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Substitute for form 1449A/PTO  
 (Modified)

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet	1	of	7	Attorney Docket Number	014643-012110US (A-72018/455675-83)
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### Complete if Known

Application Number	10/000,433
Filing Date	November 30, 2001
First Named Inventor	TOMIZUKA, Kazuma
Group Art Unit	
Examiner Name	

### U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.	U.S. Patent Document Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
A1	5,175,384		12-1992	Krimpenfort	
A2	5,204,244		04-1993	Fell et al.	
A3	5,416,260		05-1995	Jikker	
A4	5,434,340		07-1995	Krimpenfort	
A5	5,545,806		08-1996	Lonberg et al.	
A6	5,545,807		08-1996	Surani	
A7	5,569,825		10-1996	Lonberg et al.	
A8	5,625,126		04-1997	Lonberg et al.	
A9	5,633,425		05-1997	Lonberg et al	
A10	5,661,016		08-1997	Lonberg et al	
A11	5,698,196		12-1997	Matsushima	
A12	5,702,946		12-1997	Doerschuk	
A13	5,770,429		06-1998	Lonberg et al.	
A14	5,789,650		08-1998	Lonberg et al.	
A15	5,814,318		09-1998	Lonberg et al.	
A16	5,939,598		08-1999	Kucherlapati et al.	
A17	5,874,299		02-1999	Lonberg et al.	
A18	5,877,397		03-1999	Lonberg et al.	
A19	6,300,129		10-2001	Lonberg et al	

### FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.	Foreign Patent Document Country Code <sup>2</sup> Number <sup>3</sup> Kind Code <sup>4</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>5</sup>
	B1	EP 0 315 062 ✓	05-1989			
	B2	WO 90/04036 ✓	04-1990			
	B3	WO 90/12878 ✓	11-1990			
	B4	WO 91/00906 ✓	01-1991			
	B5	WO 91/10741 ✓	07-1991			
	B6	WO 92/03918 ✓	03-1992			
	B7	WO 96/02576 ✓	02-1996			

Examiner Signature		Date Considered	6/17/05
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Application Number	10/000,433				
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Group Art Unit					
Examiner Name					
Sheet	2	of	7	Attorney Docket Number	014643-012110US (A-72018/455675-83)

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

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## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
✓	C1	ALT, F.W., et al., "Immunoglobulin genes in transgenic mice", <i>Trends in Genetics</i> , 231-236, (Aug. 1985).
✓	C2	BERMAN, J.E., et. al., "Content and organization of the human Ig V <sub>H</sub> locus: definition of three new V <sub>H</sub> families and linkage to the Ig C <sub>H</sub> locus", <i>The EMBO J.</i> 7:727-738 (1988).
✓	C3	BERTON, M.T., et. al., "Synthesis of germ-line $\gamma$ 1 immunoglobulin heavy-chain transcripts in resting B cells: Induction by interleukin 4 and inhibition by interferon $\gamma$ ", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 86:2829-2833 (1989).
✓	C4	BOLLAG, R.J., et al., "Homologous recombination in mammalian cells", <i>Annu. Rev. Genet.</i> 23:199-225 (1989).
✓	C5	BRUGGEMANN, M., et al., "A repertoire of monoclonal antibodies with human heavy chains from transgenic mice", <i>Proc. Natl. Acad. Sci. USA</i> 86:6709-6713 (1989).
✓	C6	BRUGGEMANN, M., et al., "Human antibody production in transgenic mice: expression from 100 kb of the human IgH locus", <i>Eur. J. Immunol.</i> 21:1323-1326 (1991).
✓	C7	BUCCINI, D., et al., "Rearrangement of a chicken immunoglobulin gene occurs in the lymphoid lineage of transgenic mice", <i>Nature</i> 326:409-411 (1987).
✓	C8	BUTTIN, G., "Exogenous Ig gene rearrangement in transgenic mice: a new strategy for human monoclonal antibody production?" <i>Trends in Genetics</i> --vol. 3, No. 8, 205-206 (Aug. 1987).
✓	C9	CAPECCHI, M.R., "Altering the genome by homologous recombination", <i>Science</i> 244:1288-1292 (1989).
✓	C10	CAPECCHI, M.R., "The new mouse genetics: Altering the genome by gene targeting", <i>Trends in Genetics</i> 5:70-76 (1989).
✓	C11	CHOI, T.K., et al., "Transgenic mice containing a human heavy chain immunoglobulin gene fragment cloned in a yeast artificial chromosome." <i>Nat Genet.</i> 1993 Jun;4(2):117-23.
✓	C12	COFFMAN, R.L., et al., "A mouse T cell product that preferentially enhances IgA production", <i>J. Immunol.</i> 139:3685-3690 (1987).
✓	C13	COFFMAN, R.L., and CARTY, J, "A T cell activity that enhances polyclonal IgE production and its inhibition by interferon- $\gamma$ ", <i>J. Immunol.</i> 136:949-954 (1986).
✓	C14	DAVIES, N.P., et al., "Creation of Mice Expressing Human Antibody Light Chains by Introduction of a Yeast Artificial Chromosome Containing the Core Region of the Human Immunoglobulin $\kappa$ Locus." <i>Biotechnology (N Y)</i> . 1993 Aug;11(8):911-4.
✓	C15	DAVIES, N.P., et al., "Targeted Alterations in Yeast Artificial Chromosomes for Inter-Species Gene Transfer", <i>Nucleic Acid Res.</i> 20: 2693-2698 (1992).
✓	C16	DOETSCHMAN, T., et al., "Targetted correction of a mutant HPRT gene in mouse embryonic stem cells", <i>Nature</i> 330:576-578 (1987).
✓	C17	DURDIK, J., et al., "Isotype switching by a microinjected $\mu$ immunoglobulin heavy chain gene in transgenic mice", <i>Proc. Natl. Acad. Sci. USA</i> 86:2346-2350 (1989).
✓	C18	ESSER, C., and RADBRUCH, A., "Rapid induction of transcription of unarranged Sy1 switch regions in activated murine B cells by interleukin 4", <i>The EMBO J.</i> 8:483-488 (1989).
✓	C19	FERRIER, P., et al., "Separate elements control DJ and VDJ rearrangement in a transgenic recombination substrate", <i>The EMBO J.</i> 9:117-125 (1990).

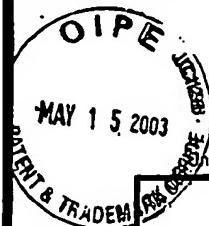
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Substitute for form 1449A/PTO (Modified)					
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>					
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Sheet	3	of	7	Attorney Docket Number	014643-012110US (A-72018/455675-83)

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**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
✓	C20	FISHWILD, D.M., et al. "High-Avidity human IgG <sub>κ</sub> monoclonal antibodies from a novel strain of minilocus transgenic mice", <i>Nature Biotechnology</i> 14:845. (1996).
✓	C21	FORNI, L., "Extensive splenic B cell activation in IgM-transgenic mice", <i>Eur. J. Immunol.</i> 20:983-989 (1990).
✓	C22	GERSTEIN, R.M., et al. "Isotype Switching of an Immunoglobulin Heavy Chain Transgene Occurs by DNA Recombination between Different Chromosomes", <i>Cell</i> 63:537-548 (1990).
✓	C23	GOODHARDT, M., et al. "Rearrangement and expression of rabbit immunoglobulin κ light chain gene in transgenic mice", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 84:4229-4233 (1987).
	C24	GORDON, J., "Transgenic mice in immunology", <i>The Mount Sinai Journal of Medicine</i> , 53:223-231 (1986).
✓	C25	GREEN, L.L., et al. "Antigen-specific human monoclonal antibodies from mice engineered with human Ig heavy and light chain YACs", <i>Nature Genetics</i> 7:13-21 (1994).
✓	C26	HAGMAN, J., et al. "Inhibition of immunoglobulin gene rearrangement by the expression of a λ2 transgene", <i>J. Exp. Med.</i> 169:1911-1929 (1989).
✓	C27	HOFKER, M.H., et al. "Complete physical map of the human immunoglobulin heavy chain constant region gene complex", <i>Proc. Natl. Acad. Sci. USA</i> 86:5567-5571 (1989).
✓	C28	HUMPHRIES, C.G., et al. "A new human immunoglobulin V <sub>H</sub> family preferentially rearranged in immature B-cell tumours", <i>Nature</i> 331:446-449 (1988).
✓	C29	HUXLEY, C., et al. "The human HPRT gene on a yeast artificial chromosome is functional when transferred to mouse cells by cell fusion." <i>Genomics</i> 1991 Apr;9(4):742-50.
✓	C30	ICHIHARA, Y., et al. "Organization of human immunoglobulin heavy chain diversity gene loci", <i>The EMBO J.</i> 7:4141-4150 (1988).
✓	C31	IGLESIAS, A., et al. "Expression of immunoglobulin delta chain causes allelic exclusion in transgenic mice", <i>Nature</i> 330:482-484 (1987).
✓	C32	JAENISCH, R., "Transgenic Animals", <i>Science</i> 240:1468-1474 (1988).
	C33	JAKOBOWITS, A., et al. "Analysis of homozygous mutant chimeric mice: Deletion of the immunoglobulin heavy-chain joining region blocks B-cell development and antibody production", <i>Proc. Natl. Acad. Sci. USA</i> 90:2551-2555 (1993).
✓	C34	JAMES, K., and BELL, G.T., "Human monoclonal antibody production current status and future prospects", <i>J. of Immunol. Methods</i> 100:5-40 (1987).
✓	C35	JASIN, M., and BERG, P., "Homologous integration in mammalian cells without target gene selection", <i>Genes &amp; Development</i> 2:1353-1363 (1988).
✓	C36	JUNG, S., et al. "Shutdown of Class Switching Recombination by Deletion of a Switch Region Control Element", <i>Science</i> 259:984-987 (1993).
✓	C37	KENNY, J.J., et al. "Alteration of the B cell surface phenotype, immune response to phosphocholine and the B cell repertoire in M167 μ plus κ transgenic mice", <i>J. of Immunol.</i> 142:4466-4474 (1989).
✓	C38	KITAMURA, D., et al. "A B cell-deficient mouse by targeted disruption of the membrane exon of the immunoglobulin μ chain gene", <i>Nature</i> 350:423-426 (1991).

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(Modified)INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

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Sheet	4	of	7	Attorney Docket Number	014643-012110US (A-72018/455675-83)
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Application Number	10/000,433
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## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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✓	C39	KOLLER, B.H., and SMITHIES, O., "Inactivating the $\beta_2$ -microglobulin locus in mouse embryonic stem cells by homologous recombination", <i>Proc. Natl. Acad. Sci. USA</i> 86:8932-8935 (1989).
✓	C40	LIN, F.L., et al., "Recombination in mouse L cells between DNA introduced into cells and homologous chromosomal sequences", <i>Proc. Natl. Acad. Sci. USA</i> 82:1391-1395 (1985).
✓	C41	LINTON, P.-J., et al., "Primary Antibody-Forming Cells and Secondary B Cells Are Generated from Separate Precursor Cell Subpopulations", <i>Cell</i> 59:1049-1059 (1989).
✓	C42	LO, D., et al., "Expression of mouse IgA by transgenic mice, pigs and sheep", <i>Eur. J. Immunol.</i> 21:1001-1006 (1991).
✓	C43	LONBERG, M., et al., "Antigen-specific human antibodies from mice comprising four distinct genetic modifications", <i>Nature</i> 368:856-859 (1994).
✓	C44	LORENZ, W., et al., "Physical map of the human immunoglobulin $\kappa$ locus and its implications for the mechanisms of $V\kappa$ - $J\kappa$ rearrangement", <i>Nucl. Acids Res.</i> 15:9667-9676 (1987).
✓	C45	LUTZKER, S., and ALT, F.W., "Structure and Expression of Germ Line Immunoglobulin $\gamma$ 2b Transcripts", <i>Mol. Cell Biol.</i> 8:1849-1852 (1988).
✓	C46	MANSOUR, S.L., et al., "Disruption of the proto-oncogene <i>int-2</i> in mouse embryo-derived stem cells: a general strategy for targeting mutations to non-selectable genes", <i>Nature</i> 336:348-352 (1988).
✓	C47	MILLER, J., et al., "Structural alterations in J regions of mouse immunoglobulin $\lambda$ genes are associated with differential gene expression", <i>Nature</i> 295:428-430 (1982).
✓	C48	MILLS, F.C., et al., "DNase I hypersensitive sites in the chromatin of human $\mu$ Immunoglobulin heavy-chain genes", <i>Nature</i> 306:809-812 (1983).
✓	C49	MILLS, F.C., et al., "Sequences of human immunoglobulin switch regions: implications for recombination and transcription", <i>Nucl. Acids. Res.</i> 18:7305-7316 (1991).
✓	C50	MORRISON, S.L., "Success in specification", <i>Nature</i> 368:812-813 (1994).
✓	C51	MOWATT, M.R., et al., "DNA sequence of the murine $\gamma$ 1 switch segment reveals novel structural elements", <i>J. Immunol.</i> 136:2674-2683 (1986).
✓	C52	MÜLLER, W., et al., "Membrane-bound IgM obstructs B cell development in transgenic mice", <i>Eur. J. Immunol.</i> 19:923-928 (1989).
✓	C53	MURRAY, A.W., and SZOSTAK, J.W., "Construction of artificial chromosomes in yeast", <i>Nature</i> 305:189-193 (1983).
✓	C54	NIKAIDO, T., et al., "Nucleotide Sequences of Switch Regions of Immunoglobulin C and C Genes and Their Comparison", <i>J. Biol. Chem.</i> 257:7322-7239 (1982).
✓	C55	NIKAIDO, T., et al., "Switch region of immunoglobulin C $\mu$ gene is composed of simple tandem repetitive sequences", <i>Nature</i> 292:845-848 (1981).
✓	C56	NEUBERGER, M.S., et al., "Isotype exclusion and transgene down-regulation in immunoglobulin- $\lambda$ transgenic mice", <i>Nature</i> 338:350-352 (1989).
✓	C57	NEUBERGER, M.S., "Generating high-avidity human Mabs in mice", <i>Nature Biotechnology</i> 14:826 (1996).
✓	C58	NUSSENZWEIG, M.C., et al., "Allelic exclusion in transgenic mice carrying mutant human IgM genes", <i>J. Exp. Med.</i> 167:1969 (1988).

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				Group Art Unit	1632
				Examiner Name	LI, Q. Janice
				Attorney Docket Number	014643-012110US/ A-72018/GKS/THR

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

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X	C115	KAZUKI, Y., et al., "Germline transmission of a transferred human chromosome 21 fragment in transchromosomal mice," <i>J. Hum. Genet.</i> 46(10):600-603 (2001).
	C116	KUROIWA, Y., et al., "Cloned transchromosomal calves producing human immunoglobulin," <i>Nat. Biotechnol.</i> 20(9):889-894 (Sep. 2002).
	C117	KUROIWA, Y., et al., "Efficient modification of a human chromosome by telomere-directed truncation in high homologous recombination-proficient chicken DT40 cells," <i>Nucleic Acid Res.</i> 26(14):3447-3448 (Jul. 1998).
	C118	KUROIWA, Y., et al., "Manipulation of human minichromosomes to carry greater than megabase-sized chromosome inserts," <i>Nat. Biotechnol.</i> 18(10):1086-1090 (Oct. 2000).
	C119	KUROIWA, Y., et al., "The use of chromosome-based vectors for animal transgenesis," <i>Gene Ther.</i> 9(11):708-712 (Jun. 2002).
	C120	ROBL, J.M., et al., "Artificial chromosome vectors and expression of complex proteins in transgenic animals," <i>Theriogenology</i> 59:107-113 (2003).
	C121	SANO, T., et al., "Transgenic potato expressing a double-stranded RNA-specific ribonuclease is resistant to potato spindle tuber viroid," <i>Nat. Biotechnol.</i> 15(12):1290-1294 (Nov. 1997).
X	C122	SHINOHARA, T., et al., "Stability of transferred human chromosome fragments in cultured cells and in mice," <i>Chromosome Res.</i> 8(8):713-725 (2000).
	C123	TOMIZUKA, K., et al., "Double trans-chromosomal mice: Maintenance of two individual human chromosome fragments containing Ig heavy and κ loci and expression of fully human antibodies," <i>Proc. Natl. Acad. Sci. USA</i> 97(2):722-727 (Jan. 2000).
	C124	TOMIZUKA, K., et al., "Functional expression and germline transmission of a human chromosome fragment in chimaeric mice," <i>Nat. Genet.</i> 16(2):134-143 (Jun. 1997).
X	C125	VON BOEHMER, et al., "Early expression of a T-cell receptor β-chain transgens suppresses rearrangement of the Vγ4 gene segment," <i>Proc. Natl. Acad. Sci. USA</i> 85(24):9729-9732 (Dec. 1988).

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Substitute for form 1449A/PTO (Modified)				Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				Application Number	10/000,433
Sheet	5	of	7	Filing Date	November 30, 2001
				First Named Inventor	TOMIZUKA, Kazuma
				Group Art Unit	
				Examiner Name	
				Attorney Docket Number	014643-012110US (A-72018/455675-83)

### OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
✓	C59	NUSSENZWEIG, M.C., et al., "A human immunoglobulin gene reduces the incidence of lymphomas in c-Myc-bearing transgenic mice", <i>Nature</i> 336:446-450 (1988).
✓	C60	NETTINGER, M.A., et al., "RAG-1 and RAG-2, Adjacent Genes That Synergistically Activate V(D)J Recombination", <i>Science</i> 248:1517-1523 (1990).
✓	C61	PETTERS, R.M., "Transgenic mice in immunological research", <i>Vet. Immunol. Immunopath.</i> 17:267-278 (1987).
✓	C62	PETTERSSON, S., et al., "A second B cell-specific enhancer 3' of the immunoglobulin heavy-chain locus", <i>Nature</i> 344:165-168 (1990).
✓	C63	RABBITS, T.H., et al., "Human immunoglobulin heavy chain genes: evolutionary comparisons of C $\mu$ , C $\delta$ and C $\gamma$ genes and associated switch sequences", <i>Nucl. Acids Res.</i> 9:4509-4524 (1981).
✓	C64	RATH, S., et al., "B cell abnormalities induced by a $\mu$ Ig transgene extend to L chain isotype usage", <i>J. of Immunol.</i> 146:2841 (1991).
✓	C65	RATH, S., et al., "Quantitative analysis of idiotypic mimicry and allelic exclusion in mice with a $\mu$ Ig Transgene", <i>J. of Immunol.</i> 143:2074-2080 (1989).
✓	C66	RAVETCH, J.V., et al., "Evolutionary approach to the question of immunoglobulin heavy chain switching: Evidence from cloned human and mouse genes", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 77:6734-6738 (1980).
✓	C67	REID, L.E., et al., "A single DNA response element can confer inducibility by both $\alpha$ - and $\gamma$ -interferons", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 86:840-844 (1989).
✓	C68	RITCHIE, K.A., et al., "Allelic exclusion and control of endogenous immunoglobulin gene rearrangement in $\kappa$ transgenic mice", <i>Nature</i> 312:517-520 (1984).
✓	C69	ROTHMAN, P., et al., "Structure and expression of germline immunoglobulin $\gamma$ 3 heavy chain gene transcripts: implications for mitogen and lymphokine directed class-switching", <i>Intl. Immunol.</i> 2:621-627 (1990).
✓	C70	RUSCONI, S., et al., "Transmission and expression of a specific pair of rearranged immunoglobulin $\mu$ and $\kappa$ genes in a transgenic mouse line", <i>Nature</i> 314:330-334 (1985).
✓	C71	SATO, T., et al., "Physical linkage of a variable region segment and the joining region segment of the human immunoglobulin heavy chain locus", <i>Biochem. Biophys. Res. Comm.</i> 154:264-271 (1988).
✓	C72	SCANGOS, G., and BIEBERICH, C., "Gene transfer into mice", <i>Advances in Genetics</i> 24: 285-322 (1987).
✓	C73	SEVIDY, J.M., and SHARP, P.A., "Positive genetic selection for gene disruption in mammalian cells by homologous recombination", <i>Proc. Natl. Acad. Sci. USA</i> 86:227-231 (1989).
✓	C74	SHIMIZU, A., et al., "Immunoglobulin double-isotype expression by trans-mRNA in a human immunoglobulin transgenic mouse", <i>Proc. Natl. Acad. Sci. USA</i> 86:8020-8023 (1989).
✓	C75	SHIMIZU, A., et al., "Trans-Splicing as a Possible Molecular Mechanism for the Multiple Isotype Expression of the Immunoglobulin Gene", <i>J. Exp. Med.</i> 173:1385-1393 (1991).
✓	C76	SHIN, E. K., et al., "Physical Map of the 3' Region of the Human Immunoglobulin Heavy Chain Locus: Clustering of Autoantibody-reacted Variable Segments In One Haplotype", <i>The EMBO J.</i> : 10, 3641-3645 (1991).
✓	C77	SIDERAS, P., et al., "Production of sterile transcripts by C $\gamma$ genes in an IgM-producing human neoplastic B cell line that switches to IgG-producing cells", <i>Intl. Immunol.</i> 1: 631-642 (1989).
✓	C78	SIEBENLIST, U., et al., "Human immunoglobulin D segments encoded in tandem multigenic families", <i>Nature</i> 294:631-635 (1981).

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Sheet	6	of	7	Attorney Docket Number	014643-012110US (A-72018/455675-83)
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Application Number	10/000,433
Filing Date	November 30, 2001
First Named Inventor	TOMIZUKA, Kazuma
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✓	C79	SMITHIES, O., et al., "Insertion of DNA sequences into the human chromosomal $\beta$ -globin locus by homologous recombination", <i>Nature</i> 317:230-234 (1985).	
✓	C80	SNAPPER, C.M., and Paul, W.E., "Interferon- $\gamma$ and B Cell Stimulatory Factor-1 Reciprocally Regulate Ig Isotype Production", <i>Science</i> 236:944-947 (1987).	
✓	C81	SONG, K.-Y., et al., "Accurate modification of a chromosomal plasmid by homologous recombination in human cells", <i>Proc. Natl. Acad. Sci. USA</i> 84:6820-6824 (1987).	
✓	C82	STAVNEZER, J., et al., "Immunoglobulin heavy-chain switching may be directed by prior induction of transcripts from constant-region genes", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 85:7704-7708 (1988).	
✓	C83	STORB, U., et al., "Expression, Allelic Exclusion and Somatic Mutation of Mouse Immunoglobulin Kappa Genes", <i>Immunological Reviews</i> 89:85-102 (1986).	
✓	C84	STORB, U., "Immunoglobulin Gene Analysis in Transgenic Mice, in <i>Immunoglobulin Genes</i> , Academic Press Limited, pp. 303-326 (1989).	
✓	C85	SZUREK, P., et al., "Complete nucleotide sequence of the murine $\gamma$ 3 switch region and analysis of switch recombination in two $\gamma$ 3-expressing hybridomas", <i>J. Immunol.</i> 135:620-626 (1985).	
✓	C86	TAHARA, T., et al., "HLA antibody responses in HLA class I transgenic mice", <i>Immunogenetics</i> 32:351-360 (1990).	
✓	C87	TAKAI, T., et al., "Augmented Humoral and Anaphylactic Responses in Fc $\gamma$ RII-deficient Mice", <i>Nature</i> 379:346-349 (1996).	
✓	C88	TAKI, S., et al., "Targeted Insertion of a Variable Region Gene into the Immunoglobulin Heavy Chain Locus", <i>Science</i> 262:1268-1271 (1993).	
✓	C89	TANAKA, T., et al., "An Antisense Oligonucleotide Complementary to a Sequence in Ig $\gamma$ b Increase $\gamma$ b Germline Transcripts, Stimulates B cell DNA Synthesis, and Inhibits Immunoglobulin Secretion", <i>The Journal of Experimental Medicine</i> 175:597-607 (1992).	
✓	C90	TAUSSIG, M.J., et al., "Regulation of immunoglobulin gene rearrangement and expression", <i>Immunology Today</i> 10:143-146 (1989).	
✓	C91	TAYLOR, L.D., et al., "Human immunoglobulin transgenes undergo rearrangement, somatic mutation and class switching in mice that lack endogenous IgM", <i>International Immunology</i> 6:579-591 (1994).	
✓	C92	THOMAS, K.R., and CAPECCHI, M.R., "Site-Directed Mutagenesis by Gene Targeting in Mouse Embryo-Derived Stem Cells", <i>Cell</i> 51:503-512 (1987).	
✓	C93	THOMAS, K.R., et al., "High Frequency Targeting of Genes to Specific Sites in the Mammalian Genome", <i>Cell</i> 44:419-428 (1986).	
✓	C94	TOMIZUKA, K., et al., "Double Trans-Chromosomal Mice: Maintenance of Two Individual Human Chromosome Fragments Containing Ig Heavy and Kappa Loci and Expression of Fully Human Antibodies," <i>Proc. Nat. Acad. Sci. (USA)</i> 97:722-727 (2000)	
✓	C95	UHLMANN, E., and PEYMAN, A., "Antisense Oligonucleotides: A new therapeutic principle," <i>Chemical Reviews</i> 90:544-584 (1990).	
✓	C96	VLASOV, et al., "Arrest of immunoglobulin G mRNA translation in vitro with an alkylating antisense oligonucleotide derivative", <i>Chemical Abstracts</i> , p. 28, 112:229433X (1990).	
✓	C97	WAGNER, S.D., et al., "Antibodies generated from human immunoglobulin miniloci in transgenic mice." <i>Nucleic Acids Res.</i> 1994 Apr 25;22(8):1389-93.	

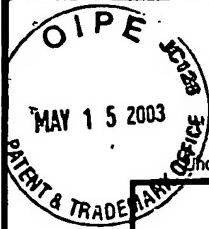
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✓	C98	WEAVER, D., et al., "A Transgenic Immunoglobulin Mu Gene Prevents Rearrangement of Endogenous Genes", <i>Cell</i> 42:117-127 (1985).	
✓	C99	WEISS, R., "Mice Making Human-Like Antibodies", <i>The Washington Post</i> , Apr. 28, 1994.	
✓	C100	YAMAMURA, K.-I., et al., "Cell-type-specific and regulated expression of a human $\gamma 1$ heavy-chain immunoglobulin gene in transgenic mice", <i>Proc. Natl. Acad. Sci. USA</i> 83:2152-2156 (1986).	
✓	C101	YANCOPOULOS, G.D., and ALT, F.W., "Developmentally Controlled and Tissue-Specific Expression of Unrearranged $V_H$ gene segments", <i>Cell</i> 40:271-281 (1985).	
✓	C102	YANCOPOULOS, G.D., and ALT, F.W., "Regulation of the Assembly and Expression of Variable-Region Genes", <i>Ann. Rev. Immunol.</i> 4:339-368 (1986).	
✓	C103	YASUI, H., et al., "Class switch from $\mu$ to $\delta$ is mediated by homologous recombination between $\sigma$ , and $\Sigma$ , sequences in human immunoglobulin gene loci", <i>Eur. J. Immunol.</i> 19:1399-1403 (1989).	
✓	C104	ZIJLSTRA, M., et al., "Germ-line transmission of a disrupted $\beta_2$ -microglobulin gene produced by homologous recombination in embryonic stem cells", <i>Nature</i> 342:435-438 (1989).	
✓	C105	ZIMMER, A., and GRUSS, P., "Production of chimaeric mice containing embryonic stem (ES) cells carrying a homeobox <i>Hox</i> 1.1 allele mutated by homologous recombination", <i>Nature</i> 338:150-153 (1989).	

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